

09/539382

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FILE 'HOME' ENTERED AT 11:08:12 ON 06 FEB 2002

=> file medline embase scisearch cancer lit

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FILE 'SCISEARCH' ENTERED AT 11:09:48 ON 06 FEB 2002

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FILE 'CANCERLIT' ENTERED AT 11:09:48 ON 06 FEB 2002

=> s "B cell lymphoma"

L1 17481 "B CELL LYMPHOMA"

=> s L1 and idiotope!

L2 11 L1 AND IDIOTOPE!

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 6 DUP REM L2 (5 DUPLICATES REMOVED)

=> d l3 1-6 bib ab

L3 ANSWER 1 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 1998095260 EMBASE

TI Autoimmunity and B-cell malignancies.

AU Dighiero G.

CS G. Dighiero, U. d'Immuno-Hematol./d'Immunopathol., Institut Pasteur, 28, rue du Dr Roux, F-75724 Paris Cedex 15, France

SO Hematology and Cell Therapy, (1998) 40/1 (1-9).

Refs: 104

ISSN: 1269-3286 CODEN: HCTHFA

CY France

DT Journal; General Review

FS 016 Cancer

025 Hematology

LA English

SL English; French

AB There is evidence indicating that autoreactive B cells constitute a substantial part of the B-cell repertoire. This autoreactive repertoire secrete the so called natural autoantibodies characterized by their broad reactivity mainly directed against very well conserved public epitopes. They fulfill the definition of an autoantibody since they are

self-reactive, but they are not selfspecific. As yet, NAA directed against determinants of polymorphism have not been reported. Their germinal origin is suggested by their early appearance during ontogeny, their expression of cross-reactive \*\*\*idiotypes\*\*\* and structural studies of their sequence. As for the physiological role of the repertoire, we can assume that it may play a major role as a first barrier of defense. It is presently unknown whether these polyreactive B cells could constitute a pre-immune template which through an antigen driven process may be involved in the production of immune high affinity antibodies. This autoreactive B cell repertoire frequently undergoes malignant transformation, although there is controversy concerning the reasons accounting for this. It has been postulated that the continuous challenge of this autoreactive repertoire by self-antigens could create propitious conditions for malignant transformation to occur. However, it can be alternatively postulated, that overexpression of certain genes reflect what happens during ontogeny, since V genes expression is a developmentally regulated phenomenon and not all V genes are expressed during fetal life. Some of the genes that are recurrently expressed by these malignancies are also over-expressed in fetal repertoires and even in the adult normal B cell repertoire. We do not know whether it is the challenge by self-antigens or whether alternatively this over-expression simply reflects what happens with the fetal repertoire which could have selective advantages for malignization.

L3 ANSWER 2 OF 6 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 91:337774 SCISEARCH  
 GA The Genuine Article (R) Number: FQ773  
 TI NUCLEOTIDE-SEQUENCE ANALYSIS OF THE V-REGIONS OF 2 IGM COLD AGGLUTININS - EVIDENCE THAT THE VH4-21 GENE SEGMENT IS RESPONSIBLE FOR THE MAJOR CROSS-REACTIVE IDIOTYPE  
 AU PASCUAL V; VICTOR K; LELSZ D; SPELLERBERG M B; HAMBLIN T J; THOMPSON K M; RANDEN I; NATVIG J; CAPRA J D (Reprint); STEVENSON F K  
 CS UNIV TEXAS, SW MED CTR, DEPT MICROBIOL, 5323 HARRY HINES BLVD, DALLAS, TX, 75235; UNIV TEXAS, SW MED CTR, DEPT INTERNAL MED, DALLAS, TX, 75235; INST IMMUNOL & RHEUMATOL, OSLO 1, NORWAY; SOUTHAMPTON GEN HOSP, TENOVUS RES LAB, LYMPHOMA RES UNIT, SOUTHAMPTON SO9 4XY, HANTS, ENGLAND  
 CYA USA; NORWAY; ENGLAND  
 SO JOURNAL OF IMMUNOLOGY, (1991) Vol. 146, No. 12, pp. 4385-4391.  
 DT Article; Journal  
 FS LIFE  
 LA ENGLISH  
 REC Reference Count: 32  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB Cold agglutinins are human autoantibodies, usually of the IgM class, which agglutinate RBC at low temperature. The major subset recognizes the I/i carbohydrate Ag, and many of these antibodies bear cross-reacting idiotypic determinants. An anti-idiotypic mAb that is specific for one of the \*\*\*idiotypes\*\*\* largely confined to cold agglutinins has been used to identify and monitor tumor cells that secrete these molecules in two patients. The tumor cells were immortalized with EBV and the idiotope-positive lines used to investigate the utilization of the V(H) and V(L) genes by these antibodies. Nucleotide sequence analysis of the two cold agglutinins (FS-1 and FS-2) revealed the utilization of a single common gene segment, V(H)4-21. Serologic analysis documented that only human antibodies utilizing the V(H)4-21 gene segment were reactive in the idiotope assay, other V(H)IV antibodies as well as a panel of antibodies derived from other V(H) families being negative. The D(H), J(H), V(K), and

J(K) gene segments of FS-1 and FS-2 were structurally distinct.

These data suggest that the structural basis for the cross-reactive idiotope as well as cold agglutinin activity is the V(H)4-21 gene segment. A nucleotide change in H chain CDR1 of both cold agglutinins results in the substitution of an aspartic acid residue for glycine at position 31, suggesting that this amino acid might be critical to recognition of the red cell Ag.

L3 ANSWER 3 OF 6 SCISEARCH COPYRIGHT 2002 ISI (R)  
AN 91:280005 SCISEARCH  
GA The Genuine Article (R) Number: FK945  
TI THE IMPACT OF IDIOTYPE-BASED STRATEGIES ON CANCER IMMUNITY  
AU KENNEDY R C (Reprint)  
CS SW FDN BIOMED RES, DEPT VIROL & IMMUNOL, HIV VACCINE PROGRAM, POB 28147,  
SAN ANTONIO, TX, 78284 (Reprint); UNIV TEXAS, HLTH SCI CTR, DEPT  
MICROBIOL, SAN ANTONIO, TX, 78284  
CYA USA  
SO IMMUNOLOGY AND ALLERGY CLINICS OF NORTH AMERICA, (1991) Vol. 11, No. 2,  
pp. 425-444.  
DT Article; Journal  
FS LIFE  
LA ENGLISH  
REC Reference Count: 81

L3 ANSWER 4 OF 6 MEDLINE DUPLICATE 1  
AN 89322739 MEDLINE  
DN 89322739 PubMed ID: 3509925  
TI Molecules recognized by anti-idiotypic monoclonal antibodies to the  
\*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* , BCL1.  
AU Tamura G S; McGrath M S; Weissman I L  
CS Department of Pathology, Stanford University School of Medicine, CA 94305.  
NC CA 32031 (NCI)  
SO JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY, (1987) 3 (4) 243-53.  
Journal code: AED; 8405005. ISSN: 0724-6803.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198908  
ED Entered STN: 19900309  
Last Updated on STN: 19970203  
Entered Medline: 19890831  
AB Monoclonal and polyclonal antibodies to the variable portions of antigen  
receptors (anti-idiotypes and anti- \*\*\*idiotopes\*\*\* ) are often employed  
to study the molecular nature and the biological role of these antigen  
receptors. Such antibodies are operationally defined as those antibodies  
which bind to a particular immunoglobulin but not to other immunoglobulins  
of the same class in a radioimmunoassay or ELISA. The monoclonal  
antibodies 32D1 and 31D1 were initially defined as anti-idiotypic as they  
recognized an immunoglobulin preparation from the murine \*\*\*B\*\*\*  
\*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* BCL1, but not other immunoglobulins of  
the

same isotype as assessed by a radioimmunoassay. A potential artifact in  
defining anti-idiotypic antibodies in this way is the possibility of  
copurification of antigen and antibody, resulting in the tentative  
identification of anti-antigen as anti-idiotypic. Previous studies have  
demonstrated that BCL1-IgM is involved in binding of murine leukemia virus

(MuLV), and BCL1 immunoglobulin and MuLV-gp70 apparently co-purified as an immune complex. Disruption of the immune complexes with SDS and sucrose gradient purification of the immunoglobulin was adequate to prepare BCL1 immunoglobulin free of gp70 as assessed by radioimmunoassay with the monoclonal anti-gp70 RA3-4A3. This preparation of immunoglobulin was used to show that 31D1 does not bind to BCL1 immunoglobulin, but to the contaminating gp70 in the BCL1 immunoglobulin preparation. However, MAb 32D1 was definitively proven to be anti-idiotypic as it recognized SDS sucrose density gradient purified IgM and immunoisolated heavy chain and light chain from BCL1 immunoglobulin. Several other lymphomas were recognized by mAb 32D1, including the T cell lymphoma UNCL and the \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* Balenlm17. To determine whether mAb 32D1 recognized immunospecific receptors on these lymphoma cell lines immunoprecipitation studies were performed. Immunoisolation and molecular analysis revealed that mAb 32D1 did not recognize the antigen receptor on these two cells, but instead recognized a cell-specific gp70. This observation demonstrates that monoclonal antibodies to known antigens (in this case an anti-idiotypic) can crossreact with apparently unrelated molecules. The potential significance of this cross reaction to the antigens recognized by B cell lymphomas is discussed.

L3 ANSWER 5 OF 6 MEDLINE DUPLICATE 2  
 AN 87035434 MEDLINE  
 DN 87035434 PubMed ID: 3490533  
 TI Idiotypic variant cell populations in patients with \*\*\*B\*\*\*  
 \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*  
 AU Carroll W L; Lowder J N; Streifer R; Warnke R; Levy S; Levy R  
 NC CA-010590 (NCI)  
 CA-33399 (NCI)  
 CA-34233 (NCI)  
 SO JOURNAL OF EXPERIMENTAL MEDICINE, (1986 Nov 1) 164 (5) 1566-80.  
 Journal code: I2V; 2985109R. ISSN: 0022-1007.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198612  
 ED Entered STN: 19900302  
 Last Updated on STN: 19970203  
 Entered Medline: 19861203  
 AB Using isolated idiotype (Id) protein we generated panels of antibodies in two patients with follicular lymphoma, one of whom had never received prior chemo-or radiotherapy. Flow cytometry and frozen section tissue staining of tumor with these monoclonal antibodies (mAb) revealed multiple subpopulations within each tumor. Individual mAb stained between 7% and 83% of surface Ig+ cells in the tumor samples. These subpopulations were overlapping and no single antibody recognized all the tumor cells. However, combinations of antibodies seemed to capture total tumor in both cases. In some instances, the percentage of tumor stained by a single mAb varied over time, and differed between lymph nodes sampled at the same time. Because a single species of Id protein was used to generate mAb in each case, it appears that the antibodies were directed against \*\*\*idiotopes\*\*\* variably shared by different populations within each tumor, and this was confirmed by crossblocking studies. Tumor cells from one patient were fused to a nonsecreting heteromyeloma line K6H6/B5, and most of the resulting hybrids secreted Id protein. Four mAb were used to screen the Id proteins secreted by these hybrids, and 11 different

variants (16 maximal) were found. Southern blot analysis of rearranged Ig genes was done in two hybrids and biopsy material. Identically rearranged light-chain genes were seen but it appeared as though extensive somatic variation had occurred in heavy chain genes. These studies indicate that: striking Id variation can exist at diagnosis in untreated patients, the percentage of tumor represented by an individual variant may change with time and may differ between tumor sampled from different anatomical locations, and somatic variation appears to be responsible for the observed heterogeneity. Although this degree of variation makes anti-Id antibody therapy more difficult, appropriate combinations of mAb should be more efficacious than single antibodies in such cases.

L3 ANSWER 6 OF 6 MEDLINE DUPLICATE 3  
 AN 86006820 MEDLINE  
 DN 86006820 PubMed ID: 3899906  
 TI Monoclonal anti-idiotypic antibodies against the murine \*\*\*B\*\*\*  
 \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* 38C13: characterization and use as probes  
 for the biology of the tumor in vivo and in vitro.  
 AU Maloney D G; Kaminski M S; Burowski D; Haimovich J; Levy R  
 NC CA-21223 (NCI)  
 GM-07365 (NIGMS)  
 SO HYBRIDOMA, (1985 Fall) 4 (3) 191-209.  
 Journal code: GFS; 8202424. ISSN: 0272-457X.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198511  
 ED Entered STN: 19900321  
 Last Updated on STN: 19970203  
 Entered Medline: 19851115  
 AB To establish a murine model for the monoclonal anti-idiotypic immunotherapy of \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*, a panel of rat and murine monoclonal anti-idiotypic antibodies of several different isotypes was generated against the surface immunoglobulin of the murine B cell tumor 38C13 (38C). Xenogeneic antibodies were made from fusions of rat spleen cells immunized with the 38C idiotypic. Syngeneic monoclonal anti-idiotypes were generated from mice immunized with the idiotypic conjugated to the protein carrier KLH. Small differences were noted in the ability of the antibodies to cross-block one another, but all appeared to be directed against the same or closely spaced \*\*\*idiotopes\*\*\* on the immunoglobulin molecule. The antibodies selectively precipitated surface Ig from 38C tumor cells and not from normal mouse spleen cells. They were used to selectively stain 38C tumor cells in cell suspensions for FACS analysis or immunohistochemical staining of tissue sections from mice bearing the tumor. As the malignancy progressed, the number of tumor cells found in all tissues examined increased. Thus, the anti-Id antibodies provided a specific probe for tumor cell detection. The antibodies had no detectable effect on cell growth in vitro; however, they did cause the rapid transient loss of the expression of cell surface Ig. This modulation was concentration and time dependent but not 100% complete. Re-expression of the Id occurred by 24 h following removal of the anti-Id antibodies. When these antibodies were used in sensitive radioisotope and enzyme linked immunoassays, the tumor cells were found to secrete small amounts of idiotypic in vitro and in vivo. The level of idiotypic detected in vivo correlated with tumor growth and inversely with survival. This work is an attempt to develop further an animal model system in which to test the

diagnostic and therapeutic effects of monoclonal anti-idiotypic antibodies.

=> s 11 and clonality

L4 431 L1 AND CLONALITY

=> dup rem 14

PROCESSING IS APPROXIMATELY 82% COMPLETE FOR L4

PROCESSING COMPLETED FOR L4

L5 208 DUP REM L4 (223 DUPLICATES REMOVED)

=> s 15 and immunoglobulin

L6 149 L5 AND IMMUNOGLOBULIN

=> s 16 and clones

L7 14 L6 AND CLONES

=> dup rem 17

PROCESSING COMPLETED FOR L7

L8 14 DUP REM L7 (0 DUPLICATES REMOVED)

=> d 18 1-14 bib ab

L8 ANSWER 1 OF 14 MEDLINE

AN 2001403839 MEDLINE

DN 21348348 PubMed ID: 11454985

TI Biclinality of gastric lymphomas.

AU Cabras A D; Candidus S; Fend F; Kremer M; Schulz S; Bordi C; Weirich G; Hofler H; Werner M

CS Departments of Pathology, Technische Universitat Munchen, Munchen, Germany.. ad.cabras@lrz.tum.de

SO LABORATORY INVESTIGATION, (2001 Jul) 81 (7) 961-7.

Journal code: KZ4; 0376617. ISSN: 0023-6837.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200108

ED Entered STN: 20010806

Last Updated on STN: 20010806

Entered Medline: 20010802

AB The pathogenesis and clonal evolution of gastric diffuse large \*\*\*B\*\*\*

- \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* (DLBCL) and its relationship to extranodal marginal zone \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*

(MZBL), mucosa-associated lymphoid tissue (MALT) type, are still controversial. The aim of this study was to establish the

\*\*\*clonality\*\*\* of morphologically distinct areas of gastric lymphomas as well as their genetic relationship to each other. Six gastric lymphomas, consisting of two MZBL, MALT type, two DLBCL, and two "composite" lymphomas were subjected to laser capture microdissection and subsequent PCR-based amplification of the \*\*\*immunoglobulin\*\*\* heavy chain gene. One DLBCL showed a biclonal pattern of rearranged

\*\*\*immunoglobulin\*\*\* heavy chain (IgH) genes of two different areas without evidence of a common origin. Two composite DLBCL with areas of extranodal MZBL, MALT type, were also biclonal and displayed different IgH gene rearrangements in the small-cell and in the large-cell components, respectively. Sequencing of the CDR3 region revealed unique VH-N-D and

D-N-JH junctions, thus corroborating the presence of two genuinely distinct tumor \*\*\*clones\*\*\* in each of these three cases. In contrast, the remaining three gastric lymphomas (one DLBCL and two MZBL, MALT type) showed IgH gene rearrangements in which CDR3 regions were identical in the different tumor areas. Our results suggest that gastric DLBCL may be composed of more than one tumor cell clone. Further, DLBCL may not necessarily evolve by transformation of a low-grade lymphoma, but may also originate de novo. An ongoing emergence of new tumor \*\*\*clones\*\*\* may considerably hamper molecular diagnosis and follow-up of gastric DLBCL.

- L8 ANSWER 2 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 2001:836459 SCISEARCH  
 GA The Genuine Article (R) Number: 481UU  
 TI Clonal evolution of gastric lymphoma of mucosa-associated lymphoid tissue type  
 AU Yamauchi A; Tomita Y; Miwa H; Sakamoto H; Sugiyama H; Aozasa K (Reprint)  
 CS Osaka Univ, Sch Med, Dept Pathol, 2-2 Yamadaoka, Suita, Osaka 5650871, Japan (Reprint); Osaka Univ, Sch Med, Dept Pathol, Suita, Osaka 5650871, Japan; Kagawa Med Univ, Dept Pathol 2, Kagawa, Japan; Osaka Univ, Sch Med, Dept Clin Lab Sci, Suita, Osaka 5650871, Japan  
 CYA Japan  
 SO MODERN PATHOLOGY, (OCT 2001) Vol. 14, No. 10, pp. 957-962.  
 Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.  
 ISSN: 0893-3952.  
 DT Article; Journal  
 LA English  
 REC Reference Count: 26  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB Development of multiple lesions is frequent in gastric lymphoma of mucosa-associated lymphoid tissue (MALT) type. Presence of clonal components in multiple lesions was examined on the resected samples from 18 cases by using PCR-based method for \*\*\*immunoglobulin\*\*\* heavy-chain gene rearrangement. There were two or more lesions in 10 cases, and 2 to 12 samples were obtained from each lesion. The remaining eight cases had a single large lesion, from which two to six samples were collected from separate areas from each other. A total of 86 samples were analyzed. Histologic findings in each sample were categorized as follows: proliferation of exclusively centrocyte-like cells (CCL), large cells, and combined CCL and large cells. Monoclonal or biclonal pattern (single or two bands) was observed in 42 samples, oligoclonal pattern (three or more bands) in 30, polyclonal (smear) in 11, and no products in 3. Large-cell-type lesions showed fewer bands than those with other histologic types, and 75% of cases with large-cell type had mono- or biclonal proliferation. Common \*\*\*clones\*\*\* were found among lesions in about 60% of cases. Especially in 4 cases including 2 cases with large-cell type, every lesion in the same case contained the common \*\*\*clones\*\*\*. These findings suggested that gastric MALT lymphoma started as multi- or oligoclonal proliferation of cells, in which separate lesions composed of different \*\*\*clones\*\*\* from each other. As disease advances, dominant \*\*\*clones\*\*\* appear in some lesion and disseminate to other lesions via homing properties of the proliferating B lymphocytes.
- L8 ANSWER 3 OF 14 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 2001402819 EMBASE  
 TI Immortalized Epstein-Barr virus-positive B-cell lines obtained by prolonged culture of peripheral blood mononuclear cells from human

immunodeficiency virus type 1-positive patients.

AU Ruibal-Ares B.; Belmonte L.; Bare P.; Scolnik M.; Palacios M.F.;  
Bayo-Hanza C.; Galmarini C.M.; Mendez G.; De Bracco M.M.E.

CS B. Ruibal-Ares, IIHEMA, Academia Nacional de Medicina, P. de Melo 3081,  
1425 Buenos Aires, Argentina. bhruibal@mail.retina.ar

SO Journal of Human Virology, (2001) 4/4 (200-213).  
Refs: 53  
ISSN: 1090-9508 CODEN: JHVIFC

CY United States

DT Journal; Article

FS 004 Microbiology  
016 Cancer  
025 Hematology  
026 Immunology, Serology and Transplantation

LA English

SL English

AB Objectives: To study the factors that determine malignant B cell growth in  
human immunodeficiency virus type 1 (HIV-1)-infected patients. Study  
Design: B-cell lines (lymphocyte cell lines [LCL] were developed after  
nonstimulated culture of peripheral blood mononuclear cells (PBMC) from  
HIV-1 positive (HIV-1(+)) patients. Human immunodeficiency virus type 1  
replication in culture, Epstein-Barr virus (EBV) latent oncogene  
expression, and cell-to-cell interaction were studied after nonstimulated  
culture of HIV-1(+) PBMC, analyzing their contribution to LCL appearance.  
Methods: Nonstimulated PBMC cultures of HIV-1(+) PBMC and controls  
(N-PBMC) were established. Lymphocyte cell lines were characterized.  
Epstein-Barr virus latent membrane protein 1 (LMP-1) and Epstein-Barr  
nuclear antigen 2 were detected by polymerase chain reaction (PCR).  
\*\*\*Clonality\*\*\* of LCL was determined by light chain restriction (flow  
cytometry) and \*\*\*immunoglobulin\*\*\* H chain rearrangement (semi-nested  
PCR). Peripheral blood mononuclear cell phenotypes were studied at  
different intervals of culture. Results: Lymphocyte cell lines were  
obtained in 73% of HIV-1(+) PBMC cultures, compared with 6% in N-PBMC. All  
LCL were EBV-positive (EBV(+)). B-cell lineage was established, and up to  
12 different B-cell \*\*\*clones\*\*\* were expanded from the same  
individual. Occurrence of LCL was more frequent in cultures with HIV-1  
replication, high LMP-1 expression in viable B cells, and high CD4:CD8  
ratio. Human immunodeficiency virus type 1 replication persisted in 53% of  
the LCL. Conclusions: In vitro HIV-1 replication and persistence of viable  
EBV(+) lymphoblasts favor spontaneous in vitro outgrowth of LCL in  
HIV-1(+) patients. .COPYRGT. Lippincott Williams & Wilkins, Inc.

L8 ANSWER 4 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)

AN 2001:422823 SCISEARCH

GA The Genuine Article (R) Number: 434AY

TI Active idiotypic vaccination in a patient with biclonal follicular  
lymphoma

AU Barrios Y; Plaza A; Cabrera R; Yanez R; Suarez E; Fernandez M N;  
Diaz-Espada F (Reprint)

CS Hosp Clin Puerta de Hierro, Dept Immunol, San Martin de Porres 4, Madrid  
28035, Spain (Reprint); Hosp Clin Puerta de Hierro, Dept Immunol, Madrid  
28035, Spain; Hosp Clin Puerta de Hierro, Dept Haematol, Madrid 28035,  
Spain

CYA Spain

SO CANCER IMMUNOLOGY IMMUNOTHERAPY, (APR 2001) Vol. 50, No. 2, pp. 87-92.  
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.  
ISSN: 0340-7004.



DT Article; Journal

LA English

REC Reference Count: 17

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Specific immunological responses to the idiotypic epitopes present in the surface \*\*\*immunoglobulin\*\*\* (Ig) of the clonal tumour population can be induced for active immunotherapy in patients with B-cell non-Hodgkin lymphoma (NHL). The \*\*\*clonality\*\*\* of the tumour cells should have important implications for the success of the implemented therapy. Here we report on the case of a patient enrolled in a protocol of active idiotypic immunotherapy in which previous cytofluorometric analysis showed a major IgM(+), kappa(+), population in the tumoral cell suspensions. However, sequence analysis of both tumour sample and tumour-derived hybrids revealed the presence of two unrelated \*\*\*clones\*\*\* that used different VH and VK gene segments. It was possible to obtain hybridomas secreting these two different IgM, kappa idiotypic proteins. The patient was immunised with a mixture of these two idiotypic Igs conjugated to keyhole limpet haemocyanin. Anti-idiotypic antibodies directed against both tumour-associated proteins were detected. This is the first case of anti-idiotypic therapy in a patient with a biclonal NHL. Our work calls attention to the question of \*\*\*clonality\*\*\* in the context of idiotypic vaccination in NHL patients.

L8 ANSWER 5 OF 14 MEDLINE

AN 2000106498 MEDLINE

DN 20106498 PubMed ID: 10643704

TI Oligoclonal non-neoplastic B cell expansion is the key feature of type II mixed cryoglobulinemia: clinical and molecular findings do not support a bone marrow pathologic diagnosis of indolent \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*.

AU De Vita S; De Re V; Gasparotto D; Ballare M; Pivetta B; Ferraccioli G; Pileri S; Boiocchi M; Monteverde A

CS University of Udine, Italy.

SO ARTHRITIS AND RHEUMATISM, (2000 Jan) 43 (1) 94-102.  
Journal code: 90M; 0370605. ISSN: 0004-3591.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200002

ED Entered STN: 20000209

Last Updated on STN: 20000209

Entered Medline: 20000203

AB OBJECTIVE: Type II mixed cryoglobulinemia (type II MC) is often characterized by features of indolent \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* (IBCL) found on pathologic examination of bone marrow, whereas the clinical evidence does not indicate a neoplastic disorder. To better address the issue of indolent malignant versus nonmalignant bone marrow lymphoproliferation underlying type II MC, molecular analyses of B cell \*\*\*clonality\*\*\* were performed in the present study, in conjunction with clinical and pathologic characterization. METHODS: Polymerase chain reaction DNA amplification of \*\*\*immunoglobulin\*\*\* heavy chain genes was performed in bone marrow biopsy specimens obtained from 15 selected patients with type II MC, all infected with hepatitis C virus. Five of them had also developed overt \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* (OBCL) during followup. Bone marrow features were

consistent with IBCL in 9 of the 15 patients (group 1) and with reactive lymphoplasmacytosis in 6 of the 15 (group 2). RESULTS: An oligoclonal B cell expansion was detected in 6 of 9 baseline bone marrow lesions from group 1 patients (biclonal or monoclonal expansion in the remaining 3 cases), and in 6 of 6 from group 2 patients. OBCL was always monoclonal. Selected lesions were analyzed by clonospecific hybridization and by cloning and sequence analysis in patients who had developed OBCL at followup. In 4 of 5 cases, OBCL did not originate from the dominant B cell \*\*\*clones\*\*\* that were overexpanded in the putative neoplastic baseline bone marrow lesions. OBCL \*\*\*clones\*\*\* showed significant homology with rheumatoid factor database sequences. CONCLUSION: Based on the present results, as well as on evidence from previous studies of liver lesions, oligoclonal non-neoplastic B cell proliferation in the course of chronic infection-related inflammation appears to be the key feature of type II MC. Of note, molecular evidence from target tissues supports the clinical findings both at the time of type II MC diagnosis and in cases of OBCL complication. Bone marrow pathologic findings resembling those of IBCL should thus be considered in the light of clinical and molecular evidence.

L8 ANSWER 6 OF 14 MEDLINE  
AN 2000050716 MEDLINE  
DN 20050716 PubMed ID: 10583578  
TI Genotypic and phenotypic alterations in Epstein-Barr virus-associated lymphoma.  
AU Ohshima K; Suzumiya J; Kanda M; Haraoka S; Kawasaki C; Shimazaki K; Kikuchi M  
CS Department of Pathology, School of Medicine, Fukuoka University, Fukuoka, Japan.  
SO HISTOPATHOLOGY, (1999 Dec) 35 (6) 539-50.  
Journal code: GB4; 7704136. ISSN: 0309-0167.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200001  
ED Entered STN: 20000204  
Last Updated on STN: 20000204  
Entered Medline: 20000127  
AB AIMS: Epstein-Barr virus (EBV) is associated with numerous reactive and neoplastic lymphoproliferative disorders. In vitro, EBV infection can transform B-lymphocytes and induce phenotypic alterations. This study presents the clinicopathological features of four cases with malignant lymphoma, which showed phenotypic and/or genotypic alterations during the course of the disease. METHODS AND RESULTS: To determine the type of EBV genotype, we performed polymerase chain reaction (PCR) for lymphocyte-defined membrane antigen (LYDMA) of EBV, subtype A/B and latent membrane protein (LMP)-1 deletion. In addition, we analysed the terminal repeat (TR) band of EBV and receptor genes (T-cell receptor gene, TCR; \*\*\*immunoglobulin\*\*\* gene heavy chain, IgH) for EBV-infected cell \*\*\*clonality\*\*\*. Double staining of cell markers (B, T-lymphocytes; histiocytes), and in-situ hybridization (ISH) for EBV were performed using tissues obtained during the course of the disease. The first case showed genotypic and phenotypic alterations of T-cell type to B-cell type. The first TCR rearrangement and T-cell markers (CD3+, CD4+, CD8-) were lost and IgH rearrangement and B-cell markers (CD19+, CD20+) were identified. During the course of the disease, EBV-TR bands changed in size; however,

the EBV genotype type B, LMP1 deletion type, and single LYDMA band remained the same. The initial T-cell lymphoma clone was considered to be different from the latter \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* clone. The second case showed phenotypic alterations. The first B-cell marker (CD19+, CD20+, CD68-) changed to histiocytic markers (CD19-, CD20-, CD68+). However, IgH rearrangement and EBV-TR bands remained the same throughout the course of the disease and EBV genotype type A, LMP1 deletion type, and single LYDMA band remained unchanged. The third case showed phenotypic alterations. The B-cell marker (CD20+) was lost; however, IgH rearrangement of PCR and EBV genotype remained the same. In the second and third cases, the initial lymphoma \*\*\*clones\*\*\* were considered to be same as the latter \*\*\*clones\*\*\*. The last case showed lineage alterations from Hodgkin's disease to natural killer (NK) cell leukaemia. However, EBV genotype did not change. The second case and Hodgkin's disease showed LMP expression, but the first and third cases showed no LMP, and EBNA2 was not detected in all cases. CONCLUSIONS: We report the genotypic and/or phenotypic alterations in four patients with EBV-associated lymphoma/leukaemia. However, EBV genotype did not change in all four. These findings suggest that EBV might induce the cell marker and lineage alteration in vivo, as in vitro.

L8 ANSWER 7 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 97:407893 SCISEARCH  
 GA The Genuine Article (R) Number: XA237  
 TI Genetic evidence for a clonal link between low and high-grade components in gastric MALT \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*  
 AU Peng H; Du M; Diss T C; Isaacson P G; Pan L (Reprint)  
 CS UNIV COLL LONDON, SCH MED, DEPT HISTOPATHOL, UNIV ST, LONDON WC1E 6JJ, ENGLAND (Reprint); UNIV COLL LONDON, SCH MED, DEPT HISTOPATHOL, LONDON WC1E 6JJ, ENGLAND  
 CYA ENGLAND  
 SO HISTOPATHOLOGY, (MAY 1997) Vol. 30, No. 5, pp. 425-429.  
 Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.  
 ISSN: 0309-0167.  
 DT Article; Journal  
 FS LIFE; CLIN  
 LA English  
 REC Reference Count: 31  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB High-grade MALT lymphomas often contain low-grade tumour components; both cell populations have been shown to express the same \*\*\*immunoglobulin\*\*\* light chain previously. However, the clonal link between the low and high-grade components has not been established at the genetic level. To investigate this link, we have examined low- and high-grade components microdissected from tissue sections of four high-grade gastric MALT lymphomas. PCR and sequence analyses were performed to identify clone-specific rearranged \*\*\*immunoglobulin\*\*\* heavy chain gene sequences. In each of these cases, the PCR products from the two components were identical in size by electrophoresis. Direct sequencing revealed common clone-specific \*\*\*immunoglobulin\*\*\* heavy chain gene rearrangements in both lesions of each case, providing genetic evidence for a clonal link. These results support the proposal that high-grade MALT lymphomas generally evolve from low-grade \*\*\*clones\*\*\*

L8 ANSWER 8 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)

AN 97:33226 SCISEARCH  
 GA The Genuine Article (R) Number: VZ305  
 TI Intestinal dissemination of gastric mucosa-associated lymphoid tissue lymphoma  
 AU Du M Q; Xu C F; Diss T C; Peng H Z; Wotherspoon A C; Isaacson P G (Reprint); Pan L X  
 CS UNIV LONDON UNIV COLL, SCH MED, DEPT HISTOPATHOL, ROCKEFELLER BLDG, UNIV ST, LONDON WC1E 6JJ, ENGLAND (Reprint); UNIV LONDON UNIV COLL, SCH MED, DEPT HISTOPATHOL, LONDON WC1E 6JJ, ENGLAND; IMPERIAL CANC RES FUND, LONDON WC2A 3PX, ENGLAND; HAMMERSMITH HOSP, DEPT HISTOPATHOL, LONDON W12 0HS, ENGLAND  
 CYA ENGLAND  
 SO BLOOD, (15 DEC 1996) Vol. 88, No. 12, pp. 4445-4451.  
 Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.  
 ISSN: 0006-4971.  
 DT Article; Journal  
 FS LIFE; CLIN  
 LA English  
 REC Reference Count: 43

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Despite increasing identification of concurrent gastric and intestinal lymphomas of mucosa-associated lymphoid tissue (MALT), the clonal relationship between the two tumors and their sequential development are poorly understood. It is also unknown whether the development of these concurrent tumors is closely associated with direct antigen stimulation, which is thought to play an important role in the clonal expansion of low-grade MALT lymphomas. To investigate these, we have studied six cases of concurrent gastric and intestinal MALT lymphomas by polymerase chain reaction (PCR) amplification, cloning, and sequencing of the rearranged Ig gene, a strategy that has been widely used for analysis of  
 \*\*\*clonality\*\*\* and antigen-driven properties of B-cell malignancies.

In each case, an identical or nearly identical complementarity determining region (CDR) 3 sequence was observed between the dominant \*\*\*clones\*\*\* of concurrent gastric and intestinal MALT lymphomas. In four of six cases examined, sufficient Ig variable region sequence information was obtained to permit analysis of somatic mutations. The mutation patterns in one case suggest that the intestinal lesion is secondary to the gastric tumor, and the mutation patterns in two cases indicate that the gastric and intestinal lesions are derived from different tumour subclones, which emerge after expansion of a common early tumor clone. Furthermore, three of four cases showed ongoing Ig mutations among different PCR  
 \*\*\*clones\*\*\* at each site. These results show that concurrent gastric and intestinal MALT lymphomas are derived from the same clone and suggest that the intestinal lesions result from dissemination of gastric tumours. Antigen stimulation may play a role in tumor evolution, particularly at an early stage. (C) 1996 by The American Society of Hematology.

L8 ANSWER 9 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 95:744944 SCISEARCH  
 GA The Genuine Article (R) Number: TA835  
 TI HISTOLOGICAL CONVERSION OF FOLLICULAR LYMPHOMA WITH STRUCTURAL ALTERATIONS OF T(14-18) AND \*\*\*IMMUNOGLOBULIN\*\*\* GENES  
 AU RAGHOEBIER S; BROOS L; KRAMER M H H; VANKRIEKEN J H J M; KLUINNELEMANS J C; VANOMMEN G J B; KLUIN P M (Reprint)  
 CS LEIDEN UNIV, PATHOL LAB, RIJNSBURGERWEG 10, POB 9600, 2300 RC LEIDEN,

NETHERLANDS (Reprint); LEIDEN UNIV, PATHOL LAB, 2300 RC LEIDEN,  
NETHERLANDS; LEIDEN UNIV, DEPT HEMATOL, 2300 RC LEIDEN, NETHERLANDS;  
LEIDEN UNIV, DEPT HUMAN GENET, 2300 RC LEIDEN, NETHERLANDS

CYA NETHERLANDS

SO LEUKEMIA, (OCT 1995) Vol. 9, No. 10, pp. 1748-1755.

ISSN: 0887-6924.

DT Article; Journal

FS LIFE

LA ENGLISH

REC Reference Count: 29

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB About half of the patients with follicular lymphoma will develop an aggressive \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* with morphological changes in growth pattern and cellular morphology. Changes of the immunophenotype, especially of the expression of \*\*\*immunoglobulin\*\*\* (Ig) have been documented less frequently.

Multiple

tumor samples of two patients with follicular lymphoma who developed tumor progression, were studied by Southern blot analysis for rearrangements of the Ig genes and the oncogenes BCL2 and MYC. In both patients, the general pattern of Ig gene rearrangements, especially of the Ig light-chain genes, and the structure of the t(14;18) breakpoint as assessed by the polymerase chain reacton (PRC) and fine restriction mapping, remained unaltered with time. However, both within the functional Ig heavy-chain allele and around the t(14;18) breakpoint, extensive secondary alterations took place. This indicates clonal evolution rather than the appearance of an independent lymphoma. In the first case with progression from follicular lymphoma to Burkitt's lymphoma 3 years after diagnosis, alterations were especially present 3' of the t(14;18) breakpoint. In the second patient with a change from follicular to diffuse centroblastic lymphoma 4 years after diagnosis, subsequent class switches from IgM to IgG and to defective IgH expression were accompanied by deletion of C mu sequences and a rearrangement of the MYC gene, respectively. Additionally, in both patients alterations in individual restriction sites occurred, which most likely were due to somatic mutations within both the functional IgH and translocated allele. Our data indicate that complex alterations of both the functional and non-functional IgH allele may accompany tumor progression and may erroneously suggest the appearance of independent \*\*\*clones\*\*\* by Southern blot analysis. It remains to be established whether these alterations are causative events or the consequence of genetic instability and clonal evolution.

L8 ANSWER 10 OF 14 MEDLINE

AN 95240130 MEDLINE

DN 95240130 PubMed ID: 7723393

TI Localized gastric non-Hodgkin's lymphoma of high-grade malignancy in patients with pre-existing chronic lymphocytic leukemia or immunocytoma.

AU Ott M M; Ott G; Roblick U; Linke B; Kneba M; de Leon F; Muller-Hermelink H K

CS Institute of Pathology, University of Wurzburg, Germany.

SO LEUKEMIA, (1995 Apr) 9 (4) 609-14.

Journal code: LEU; 8704895. ISSN: 0887-6924.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

OS GENBANK-S77443; GENBANK-S77444

EM 199505  
ED Entered STN: 19950605  
Last Updated on STN: 19950605  
Entered Medline: 19950523  
AB Analyses for \*\*\*clonality\*\*\* in cases of Richter's syndrome have provided evidence for a clonal evolution of high-grade lymphoma in most patients, while in others an independent cellular clone seems to exist in the secondary neoplasm. Richter's syndrome with an isolated high-grade lymphoma of the stomach has been rarely reported in patients with pre-existing B cell chronic lymphocytic leukemia (CLL). We investigated four cases of CLL or lymphoplasmacytoid immunocytoma (LPIC) with development of a localized high-grade \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* in the stomach. Southern blotting showed different rearrangements of the \*\*\*immunoglobulin\*\*\* light and heavy chain genes in the tumor cells of the low-grade lymphoma and the gastric tumor in two cases. Comparison of the DNA sequences of the CDR3 region of the \*\*\*immunoglobulin\*\*\* genes revealed different \*\*\*clones\*\*\* in another case. By means of chromosomal in situ hybridization, trisomy 3 was detected in two cases of high-grade lymphoma of the stomach, but not in the cells of the associated low-grade tumor. Our findings indicate that high-grade non-Hodgkin's lymphomas arising localized in the stomach of patients with CLL or immunocytoma are not clonally related to the pre-existing low-grade lymphoma and, therefore indeed, present true secondary neoplasms.

L8 ANSWER 11 OF 14 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
AN 95171494 EMBASE  
DN 1995171494  
TI Separate \*\*\*clones\*\*\* in concomitant multiple myeloma and a second B-cell neoplasm demonstrated by molecular and immunophenotypic analysis.  
AU Novak P.M.; Mattson J.C.; Crisan D.; Chen J.; Pulik M.D.; Decker D.  
CS Department Clinical Pathology, William Beaumont Hospital, Royal Oak, MI 48073, United States  
SO European Journal of Haematology, (1995) 54/4 (254-261).  
ISSN: 0902-4441 CODEN: EJHAEC  
CY Denmark  
DT Journal; Article  
FS 005 General Pathology and Pathological Anatomy  
016 Cancer  
025 Hematology  
LA English  
SL English  
AB The occurrence of multiple myeloma (MM) and a second B-cell neoplasm in the same patient is a rare event. We present 2 such patients, and provide evidence to support the presence of separate \*\*\*clones\*\*\* in these coexisting neoplasms. In the first case, MM became evident 14 months after the diagnosis of chronic lymphocytic leukemia (CLL). In past reports, most occurrences of this association, when investigated, have been regarded to be biclonal disease processes; however, with few exceptions, most were documented by immunologic studies alone. To establish the \*\*\*clonality\*\*\* in our case of CLL with MM, we examined both immunophenotypic data obtained by standard two-color flow cytometric analysis, and patterns of \*\*\*immunoglobulin\*\*\* gene rearrangement, using standard Southern analysis and hybridization with 32P-labelled J(H) and J(K) probes. This provided evidence for the presence in this patient of two separate monoclonal populations of B cells, manifested as light chain restrictions and gene rearrangements which differed in blood (CLL)

and bone marrow (MM) samples. In the second case, MM presented simultaneously with bone marrow lymphocytosis and abnormal peripheral lymphocytes. \*\*\*Clonality\*\*\* studies on blood were not done. Bone marrow B-cell gene rearrangement studies, however, revealed the presence of three bands in the J(K) blot of significantly different intensities, suggestive of two monoclonal populations. A monoclonal population of small cells with surface B markers and surface IgM was demonstrated by flow cytometry, while a second population of larger cells with intracytoplasmic IgG matching the patient's serum monoclonal protein was detected by immunofluorescence microscopy. The results in these 2 cases expand previous findings of the rare association of MM with a second B-cell neoplasm, and demonstrate the usefulness of molecular diagnostic investigation.

L8 ANSWER 12 OF 14 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 95367908 EMBASE  
 DN 1995367908  
 TI Nonradioactive detection of monoclonal \*\*\*immunoglobulin\*\*\* heavy chain gene rearrangement with PCR-SSCP.  
 AU Thunberg U.; Aleml M.; Sundstrom C.; Sallstrom J.  
 CS Department of Pathology, Academic Hospital, S-751 82 Uppsala, Sweden  
 SO Hematologic Pathology, (1995) 9/3-4 (141-153).  
 ISSN: 0886-0238 CODEN: HEPAEG  
 CY United States  
 DT Journal; Article  
 FS 005 General Pathology and Pathological Anatomy  
 022 Human Genetics  
 025 Hematology  
 026 Immunology, Serology and Transplantation  
 LA English  
 SL English  
 AB The rearrangement of the \*\*\*immunoglobulin\*\*\* heavy chain gene can be used as a marker of B-cell lineage and \*\*\*clonality\*\*\*. By using polymerase chain reaction (PCR) with variable-region and joining-region specific primers it is possible to detect the rearrangement of a small amount of clonal B cells, as described by several groups. The specific PCR product can be detected after amplification with gel electrophoresis and ethidium bromide staining. The DNA fragments obtained from different \*\*\*clones\*\*\* are, however; approximately of the same size, making it difficult to distinguish between the \*\*\*clones\*\*\* by simple electrophoresis and ethidium bromide staining, as described in many reports. Single-strand conformational polymorphism (SSCP) was evaluated as a method to detect specific clonal amplicons in a mixture of PCR-amplified products. Unique patterns were obtained for different B-cell \*\*\*clones\*\*\*, detectable in mixtures of 0.25% clonal cells in normal cells. It is concluded that SSCP is a valuable method for the specificity control of PCR in B-lymphocyte \*\*\*clonality\*\*\* analyses. The advantages of the described method over previously published techniques are increased specificity simplicity without radioactivity, and rapidity.

L8 ANSWER 13 OF 14 CANCERLIT  
 AN 93682349 CANCERLIT  
 DN 93682349  
 TI Flow cytometric clonal excess analysis in non-Hodgkin's lymphoma: diagnostic and clinical aspects.  
 AU Johnson A E  
 CS Lunds Universitet, Sweden.

SO Diss Abstr Int [C], (1992). Vol. 53, No. 1, pp. 77.  
ISSN: 0419-4217.

DT (THESIS)

FS ICDB

LA English

EM 199305

AB In this thesis, the clinical value of improved detection of the spread of  
\*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* with special reference to  
blood involvement has been investigated. Non-Hodgkin's lymphomas (NHL) are  
monoclonal proliferations, and B-cell lymphomas exhibit an absolutely  
specific tumor marker in the idiotypic \*\*\*immunoglobulin\*\*\* (Ig)  
expression. A more convenient measure of \*\*\*clonality\*\*\* is the  
comparatively homogeneous and light chain-restricted Ig expression.  
Assessment of \*\*\*clonality\*\*\* by analysis of Ig light-chain (kappa and  
lambda) distribution in flow cytometry, clonal excess analysis (CE), was  
used in this study. When immunological methods of detection of B-NHL were  
introduced, the expectations were that we would have a simple tool for  
increased staging precision and for definition of remission and early  
detection of relapse. Especially in high-grade malignant NHL, this  
information might be of utmost importance for the choice and duration of  
therapy. In the present study, immunological detection was found to be  
superior to conventional morphological and hematological methods in  
identifying tumor dissemination. The existence of CE in peripheral blood  
was strongly related to low-grade histology and bone marrow involvement.  
Analyses of relapse and survival in patients (pts) with localized disease  
and in remission were consistent with an indolent nature of the  
circulating lymphoma cells. CE was confirmed as a predictor of failure to  
obtain remission in pts with advanced disease. If CE in peripheral blood  
in pts with advanced high-grade NHL is a measure of circulating  
\*\*\*clones\*\*\* equivalent to those found in localized disease and in  
remission, the results indicate the coexistence of two biologically  
different cell populations. Methodological aspects of the CE analysis were  
also studied. The postulated identity of light-chain distribution in a  
normal B-cell population serves as the basis for evaluation of the  
analysis. In peripheral blood lymphocytes the light-chain distribution is  
complex, and kappa/lambda incongruity occurs due to cytophilic Ig adsorbed  
mainly to the NK cell population and the B cells themselves. The results  
indicate that enhanced resolution is obtained by analytical evaluation of  
the kappa/lambda distribution to reveal the nature of the different  
deviations.

L8 ANSWER 14 OF 14 MEDLINE

AN 92016557 MEDLINE

DN 92016557 PubMed ID: 1921459

TI Independent clonal origin of T- and B-cell \*\*\*clones\*\*\* in a composite  
lymphoma.

AU Deane M; Amlot P; Pappas H; Norton J D

CS Department of Haematology, Royal Free Hospital, London, U.K.

SO LEUKEMIA RESEARCH, (1991) 15 (9) 811-7.

Journal code: K9M; 7706787. ISSN: 0145-2126.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199111

ED Entered STN: 19920124

Last Updated on STN: 19920124



Entered Medline: 19911114

AB We present a detailed immunohistological and genotypic analysis of an unusual case in which a peripheral T-cell lymphoma, with features of Lennert's and angioimmunoblastic lymphoma, occurred after treatment of a low grade plasmacytoid lymphoma. By analysis of \*\*\*immunoglobulin\*\*\* and T-cell receptor genes, we show that the two diseases had an independent clonal origin at the level of lymphoid commitment. However, by employing a novel polymerase chain reaction-based technique for analysis of B-cell \*\*\*clonality\*\*\*, we show the persistence of a residual minor clonal B-cell population in the subsequent T-cell lymphoma. Only 2 previous cases of composite lymphoma involving B- and T-cell \*\*\*clones\*\*\* have been demonstrated by molecular analysis. This study underlines the immunophenotypic and genotypic heterogeneity of peripheral T-cell lymphomas and illustrates an unusual disease course in which a T-cell lymphoma has arisen in the context of, and perhaps as a consequence of, a \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*.

=> d his

(FILE 'HOME' ENTERED AT 11:08:12 ON 06 FEB 2002)

FILE 'MEDLINE, EMBASE, SCISEARCH, CANCERLIT' ENTERED AT 11:09:48 ON 06 FEB 2002

L1 17481 S "B CELL LYMPHOMA"  
L2 11 S L1 AND IDIOTOPE!  
L3 6 DUP REM L2 (5 DUPLICATES REMOVED)  
L4 431 S L1 AND CLONALITY  
L5 208 DUP REM L4 (223 DUPLICATES REMOVED)  
L6 149 S L5 AND IMMUNOGLOBULIN  
L7 14 S L6 AND CLONES  
L8 14 DUP REM L7 (0 DUPLICATES REMOVED)

=> s L1 and clone!

L9 775 L1 AND CLONE!

=> s L9 and (idiotype! or idiotope!)

L10 36 L9 AND (IDIOTYPE! OR IDIOTOPE!)

=> dup rem L10

PROCESSING COMPLETED FOR L10

L11 20 DUP REM L10 (16 DUPLICATES REMOVED)

=> d L11 1-20 bib ab

L11 ANSWER 1 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)  
AN 97:366556 SCISEARCH  
GA The Genuine Article (R) Number: WX542  
TI Ongoing Ig gene hypermutation in salivary gland mucosa-associated lymphoid tissue-type lymphomas  
AU Bahler D W (Reprint); Miklos J A; Swerdlow S H  
CS MONTEFIORE UNIV HOSP, DEPT PATHOL NW 628, 200 LOTHROP ST, PITTSBURGH, PA 15213 (Reprint); UNIV PITTSBURGH, SCH MED, DIV HEMATOPATHOL, PITTSBURGH, PA; UNIV PITTSBURGH, SCH MED, DEPT PATHOL, PITTSBURGH, PA  
CYA USA  
SO BLOOD, (1 MAY 1997) Vol. 89, No. 9, pp. 3335-3344.  
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE

300, PHILADELPHIA, PA 19106-3399.  
ISSN: 0006-4971.

DT Article; Journal  
FS LIFE; CLIN  
LA English

REC Reference Count: 71

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Salivary gland mucosa-associated lymphoid tissue (MALT) type lymphomas are typically indolent B-cell neoplasms that are often associated with Sjogren's syndrome. To better define the cell of origin and evaluate whether antigen receptor stimulation may be playing a role in tumor growth, the Ig heavy and light chain variable genes (VH and VL) expressed by five salivary gland MALT lymphomas were \*\*\*cloned\*\*\* and sequenced. Comparison to known germline sequences indicated that three of the lymphoma VH genes were derived from 51p1, a member of the VH1 family, while the other two used different VH gene segments from the VH3 family, 22-2B and HG19. All five of the VL genes belonged to the VkIII family, with three derived from Humkv325 and the other two from the Vg and Humkv328 genes. Numerous point mutations relative to the proposed germline genes were present in all of the lymphoma VH and VL genes. In addition, the VH and VL genes from each lymphoma showed intraclonal sequence heterogeneity indicative of ongoing somatic hypermutation. Because the process of Ig gene hypermutation is thought to occur at the germinal center stage of B cell development, these findings suggest the MALT lymphoma cell of origin may be a germinal center B cell. Selection against mutations that result in replacement of amino acids suggested that Ig stimulation may be important for lymphoma growth. The possibility that antigen receptor stimulation may be involved in the growth of salivary gland MALT lymphomas is further suggested by the noted restricted use of VH and VL gene segments. (C) 1997 by The American Society of Hematology.

L11 ANSWER 2 OF 20 MEDLINE DUPLICATE 1

AN 97276969 MEDLINE

DN 97276969 PubMed ID: 9130662

TI T cells recognize the VH complementarity-determining region 3 of the idiotypic protein of B cell non-Hodgkin's lymphoma.

AU Wen Y J; Lim S H

CS Department of Haematology, University of Wales College of Medicine, Cardiff, GB.

SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Apr) 27 (4) 1043-7.  
Journal code: EN5; 1273201. ISSN: 0014-2980.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199705

ED Entered STN: 19970602

Last Updated on STN: 19970602

Entered Medline: 19970522

AB The idiotypic protein expressed by B lymphoma cells is a clone-specific tumor antigen which may be suitable for immune targeting by T cells. In this study, we \*\*\*cloned\*\*\* the immunoglobulin heavy chain variable gene (VH) of the idiotypic protein from a patient with \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* and used a synthetic peptide of 22 amino acids corresponding to the VH complementarity-determining region (CDR)-3 of the idiotypic protein to investigate whether autologous T cells could recognize this unique peptide. We demonstrated that autologous T cells

possessing both CD4+ and CD8+ phenotypes could be propagated. The T cells were able to proliferate, secrete cytokines, and lyse autologous cells presensitized with the specific peptide in a major histocompatibility complex-dependent manner. Moreover, these CDR3 peptide-primed T cells were also able to kill autologous lymphoma cells. Our results therefore offer new perspectives for specific therapeutic vaccination for the treatment of  
 \*\*\*B\*\*\*      \*\*\*cell\*\*\*      \*\*\*lymphoma\*\*\* .

L11 ANSWER 3 OF 20 MEDLINE DUPLICATE 2  
 AN 1998116668 MEDLINE  
 DN 98116668 PubMed ID: 9455490  
 TI Idiotypic vaccine for treatment of human \*\*\*B\*\*\* - \*\*\*cell\*\*\*  
 \*\*\*lymphoma\*\*\* . Construction of IgG variable regions from single  
 malignant B cells.  
 AU Terness P; Welschof M; Moldenhauer G; Jung M; Moroder L; Kirchhoff F;  
 Kipriyanov S; Little M; Opelz G  
 CS Institute of Immunology, University of Heidelberg, Germany.  
 SO HUMAN IMMUNOLOGY, (1997 Aug-Sep) 56 (1-2) 17-27.  
 Journal code: G9W; 8010936. ISSN: 0198-8859.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199802  
 ED Entered STN: 19980224  
 Last Updated on STN: 19980224  
 Entered Medline: 19980211  
 AB Immunoglobulin \*\*\*idiotypes\*\*\* (Id) of malignant B cells represent  
 highly specific markers which can be used for vaccination.  
 PCR-amplification of immunoglobulin genes enables the rapid production of  
 large amounts of Id vaccines. However, the separate amplification and  
 subsequent recombination of heavy and light chains can lead to a loss of  
 the relevant Id. To preserve the original chain pairs, we used single  
 malignant B cells derived from an immunocytoma patient. Cytoplasm was  
 extracted and the mRNA transcribed into cDNA. The VH and VL genes were  
 then amplified by PCR and \*\*\*cloned\*\*\* into a vector for expression in  
 E. coli. Id production was checked using an anti-Id mouse monoclonal Ab  
 raised against the patient's tumor-specific IgG. One out of 3 constructs  
 expressed the relevant Id. Analysis of the first 31 light chain residues  
 revealed an identical sequence for the malignant B cells' IgG and the  
 recombinant Id construct. Exchange of either the heavy or light chain with  
 an unrelated chain resulted in loss of the Id. An unrelated sequence  
 derived from the c-myc protein is coupled to the Id vaccine. The lymphoma  
 patient was shown to have Abs to the c-myc sequence. This sequence  
 therefore, increases the Id+ Ab's antigenicity. CD spectroscopy showed an  
 alpha-helical structure for the c-myc epitope. In conclusion, a \*\*\*B\*\*\*  
 - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* autovaccine was produced containing  
 immunogenic sequences that do not alter the steric conformation of the  
 tumor-specific Id.

L11 ANSWER 4 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 96:244552 SCISEARCH  
 GA The Genuine Article (R) Number: UB443  
 TI 3RD COMPLEMENTARITY-DETERMINING REGION SEQUENCE-ANALYSIS OF LOW-GRADE  
 BRONCHUS-ASSOCIATED LYMPHOID-TISSUE LYMPHOMA - GENOTYPIC ANALYSIS REVEALS  
 HETEROGENEITY IN MATURATION  
 AU KUROSU K (Reprint); YUMOTO N; TANIGUCHI M; KURIYAMA T; MIKATA A

CS CHIBA UNIV, SCH MED, DEPT PATHOL 1, CHUO KU, 1-8-1 INOHANA, CHIBA 260, JAPAN (Reprint); CHIBA UNIV, SCH MED, DIV MOLEC IMMUNOL, CHUO KU, CHIBA 260, JAPAN; CHIBA UNIV, SCH MED, DEPT CHEST MED, CHUO KU, CHIBA 260, JAPAN  
 CYA JAPAN  
 SO LABORATORY INVESTIGATION, (MAR 1996) Vol. 74, No. 3, pp. 609-616.  
 ISSN: 0023-6837.  
 DT Article; Journal  
 FS LIFE  
 LA ENGLISH  
 REC Reference Count: 29  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB It has recently been suggested that autoimmunity may play a role in the pathogenesis of low-grade mucosa-associated lymphoid tissue lymphomas, but precise genotypic analysis of antigen binding sites of low-grade bronchus-associated lymphoid tissue (BALT) lymphomas has not been reported.

We analyzed the third complementarity determining region (CDR3) in eight cases of low-grade BALT lymphoma by 2-step PCR and sequencing analysis. All cases showed a distinct monoclonal band (about 100 base pairs) on electrophoresis. In seven cases, a single major CDR3 sequence was identified with five to nine \*\*\*clones\*\*\* among 10 vector \*\*\*clones\*\*\* being identical; and in the remaining case, two major sequences were obtained, with four \*\*\*clones\*\*\* among nine vector \*\*\*clones\*\*\* being identical.

Findings suggestive of the autoimmunity of low-grade BALT lymphoma were obtained: (1) V(H)DJ(H) rearrangements in seven of the eight lymphoma cell \*\*\*clones\*\*\* were potentially functional; (2) genotypically, two lymphoma cell \*\*\*clones\*\*\* showed 60 to 74% homology with G6 positive lymphocyte \*\*\*clones\*\*\*; and (3) five lymphoma cell \*\*\*clones\*\*\* showed 61 to 71% homology with lymphocyte \*\*\*clones\*\*\* derived from fetal liver or cord blood. In one case, the N-D-N length of the neoplastic clone was very short and lacked N nucleotides at the D-J(H) junction. Therefore, our study demonstrates genotypic heterogeneity in maturation in low-grade BALT lymphoma.

L11 ANSWER 5 OF 20 MEDLINE DUPLICATE 3  
 AN 94250911 MEDLINE  
 DN 94250911 PubMed ID: 8193363  
 TI Idiotypic vaccination against human \*\*\*B\*\*\* - \*\*\*cell\*\*\*  
 \*\*\*lymphoma\*\*\*. Rescue of variable region gene sequences from biopsy material for assembly as single-chain Fv personal vaccines.  
 AU Hawkins R E; Zhu D; Ovecka M; Winter G; Hamblin T J; Long A; Stevenson F K  
 CS Medical Research Council Laboratory of Molecular Biology, Cambridge, UK.  
 SO BLOOD, (1994 Jun 1) 83 (11) 3279-88.  
 Journal code: A8G; 7603509. ISSN: 0006-4971.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 OS GENBANK-Z31379; GENBANK-Z31398; GENBANK-Z31579  
 EM 199406  
 ED Entered STN: 19940707  
 Last Updated on STN: 19970203  
 Entered Medline: 19940627  
 AB Idiotypic determinants on neoplastic B cells could provide tumor antigens for vaccination of patients with B-cell tumors. Because this approach requires an individual vaccine for each patient, simple methods for

obtaining idiotypic antigen are desirable. Using polymerase chain reaction (PCR) with family-based V-gene and J-region primers, the variable region genes of heavy and light chains (VH and VL) of Ig have been obtained from biopsy material from 13 patients with B-cell tumors. In each case, analysis of random \*\*\*clones\*\*\* derived from the PCR product showed repeated, clonally-related sequences, whereas normal lymphoid tissue generated no repeated sequences. In 3/3 cases, the repeated sequences were found to be the same as those in a tumor-derived hybridoma. Mutational patterns in the V-genes differed among the tumors, with follicular lymphoma tending to be more highly mutated. The individual VH and VL sequences have been assembled with a flexible linker sequence to encode single-chain Fv (scFv). The scFv sequences can be \*\*\*cloned\*\*\* into bacterial expression vectors to produce protein, or into vectors suitable for direct vaccination using naked DNA. In a model system, expressed scFv protein retained all idiotypic determinants defined by a panel of five anti-idiotypic monoclonal antibodies (MoAbs). Similarly, expressed scFv proteins from two patients were shown to react with anti-idiotypic antibodies. This approach allows production of potential vaccines from surgical biopsies within 2 to 3 weeks.

L11 ANSWER 6 OF 20 MEDLINE DUPLICATE 4  
 AN 94107863 MEDLINE  
 DN 94107863 PubMed ID: 8280708  
 TI A genetic approach to idiotypic vaccination.  
 AU Hawkins R E; Winter G; Hamblin T J; Stevenson F K; Russell S J  
 CS MRC Laboratory of Molecular Biology and Centre for Protein Engineering, Cambridge, United Kingdom.  
 SO JOURNAL OF IMMUNOTHERAPY, (1993 Nov) 14 (4) 273-8.  
 Journal code: AZO; 9102704. ISSN: 1053-8550.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199402  
 ED Entered STN: 19940228  
 Last Updated on STN: 19940228  
 Entered Medline: 19940215  
 AB Treatment of cancer with vaccines is an attractive prospect, but few tumours express suitable target antigens. With B-cell lymphomas, the idiotypic immunoglobulin (Ig) of the malignant B-cell should provide a suitable target but this requires a vaccine to be created for each patient. We propose a strategy for making such vaccines: first to clone the V genes of the idiotypic Ig, and second to inject the patient with the \*\*\*cloned\*\*\* DNA (genetic immunisation) in order to elicit an immune response against the encoded Ig. We have previously shown that the V genes of the idiotypic Ig can be identified from human lymph node biopsies by polymerase chain reaction amplification, cloning, and sequencing. In this report, we show that anti-idiotypic antibodies can be elicited by direct injection of an expression vector that encodes the V genes of murine antibodies (the V genes of B1.8, a murine hybridoma or of BCL1, a murine lymphoma line). This finding suggests a simple approach to the preparation of idiotypic vaccines for patients with \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*, which also circumvents the need for adjuvants.

L11 ANSWER 7 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AN 93:39442 SCISEARCH  
 GA The Genuine Article (R) Number: KG203

TI ANTITUMOR-ACTIVITY OF IDIOTYPE-SPECIFIC, MHC-RESTRICTED TH1 AND TH2  
 \*\*\*CLONES\*\*\* INVITRO AND INVIVO  
 AU LAURITZSEN G F (Reprint); WEISS S; BOGEN B  
 CS UNIV OSLO, INST IMMUNOL & RHEUMATOL, FR QVAMSGT 1, N-0172 OSLO, NORWAY  
 (Reprint); GBF, BRAUNSCHWEIG, GERMANY  
 CYA NORWAY; GERMANY  
 SO SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (JAN 1993) Vol. 37, No. 1, pp. 77-85.  
 ISSN: 0300-9475.  
 DT Article; Journal  
 FS LIFE  
 LA ENGLISH  
 REC Reference Count: 62  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB \*\*\*Idiotypes\*\*\* (Id) can serve as individual markers on B cells;  
 therefore, cytotoxic Id-specific T cells may play a significant role in  
 immunological surveillance of Id+ B-cell tumours. We have investigated the  
 anti-tumour activity of CD4+ BALB/c Th1 and Th2 \*\*\*clones\*\*\* which  
 recognize a processed Id of the syngeneic lambda2(315) L chain in the  
 context of the class II MHC molecule I-E(d). Id-specific T cells and  
 A20/46 B lymphoma cells transfected with the lambda2(315) gene were  
 injected s.c. into the same site of BALB/c mice (Winn assay). The results  
 show that both Th1 and Th2 \*\*\*clones\*\*\* can protect against tumour  
 development. The protection was Id-specific because T cells did not  
 influence tumour development by an A20/46 B lymphoma cell line transfected  
 with the pSV2neo expression vector alone. In vitro studies showed that the  
 Th1 \*\*\*clones\*\*\* were cytotoxic to lambda2(315)-transfected B lymphoma  
 cells; by contrast, the Th2 clone was not cytotoxic in Cr-51-release assay  
 even though the Th2 cells inhibited the growth of lambda2(315) B lymphoma  
 cells. The anti-lymphoma properties of both the Th1 and Th2 \*\*\*clones\*\*\*  
 appear to involve as yet undefined cytotoxic and growth inhibiting  
 molecules.

L11 ANSWER 8 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 92252956 EMBASE  
 DN 1992252956  
 TI Crossreacting human lymphoma \*\*\*idiotypes\*\*\*  
 AU Rudders R.A.; Levin A.; Jespersen D.; Zacks J.; Delellis R.; Ranger A.;  
 Krontiris T.  
 CS Hematology-Oncology, VA Medical Center, 150 S Huntington Ave, Boston, MA  
 02130, United States  
 SO Blood, (1992) 80/4 (1039-1044).  
 ISSN: 0006-4971 CODEN: BLOOAW  
 CY United States  
 DT Journal; Article  
 FS 025 Hematology  
 026 Immunology, Serology and Transplantation  
 LA English  
 SL English  
 AB We have examined an unselected series of 72 lymphomas of diverse  
 histologies with a panel of mouse monoclonal antibodies specific for human  
 B- lymphoma-derived Ig \*\*\*idiotypes\*\*\* (anti-ids) to determine the  
 nature and extent of id/anti-id crossreactivity. The anti-id antibodies  
 were prepared from Ig isolated from seven follicular center cell lymphomas  
 by heterohybridoma technique. Thirty-six of 75 individual anti-ids  
 obtained in this manner were further selected based on their reactivity  
 with highly restricted or private idiotypic determinants. Twelve of the 72  
 (17%) lymphoma biopsies reacted with one or more of the 36 anti-ids that

detect private determinants. A pool consisting of five individual antibodies would have detected 11 of the 12 crossreacting tumors. Staining of tumor cell populations was homogeneous in the positive cases, suggesting uniform idiotype expression. If there was a segregated staining pattern, it was generally related to the presence of CD3+ T cells in the section. These follicular center cell-derived anti-ids crossreacted with follicular center cell tumors of all histologic grades with frequencies ranging from 13% to 50%. The structural basis for the crossreactivity of our lymphoma-derived private anti-ids is as yet not known. However, the reactivity of certain anti-ids with both kappa- and lambda- expressing tumors suggests a biased use of V gene segments in these crossreactive \*\*\*clones\*\*\* that is probably related to the V(H) gene. These data suggest the possibility that lymphoma may develop in a highly restricted pool of normal differentiated B cells or in B-cell subsets that express a limited repertoire of unmutated V(H) gene segments.

L11 ANSWER 9 OF 20 MEDLINE DUPLICATE 5  
 AN 92043738 MEDLINE  
 DN 92043738 PubMed ID: 1940361  
 TI Structural basis of a conserved idiotope expressed by an autoreactive human \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* . Evidence that a VH CDR3 mutation alters idiotypy and specificity.  
 AU Reidl L S; Friedman D F; Goldman J; Hardy R R; Jefferies L C; Silberstein L E  
 CS Department of Pathology, Hospital of the University of Pennsylvania, Philadelphia 19104.  
 NC R29DK39065-01 (NIDDK)  
 SO JOURNAL OF IMMUNOLOGY, (1991 Nov 15) 147 (10) 3623-31.  
 Journal code: IFB; 2985117R. ISSN: 0022-1767.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199112  
 ED Entered STN: 19920124  
 Last Updated on STN: 19920124  
 Entered Medline: 19911216  
 AB Our laboratory has previously investigated the relationship of autoimmune disease and B cell neoplasia in a patient with a diffuse, well differentiated splenic \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* and associated autoimmune hemolysis due to an anti-Pr2 antibody. EBV-immortalized B cell \*\*\*clones\*\*\*, established from this lymphoma, were shown to secrete the same pathologic anti-Pr2 antibody. The antiidiotypic mAb, RI.1, defined a private Id (IdRI.1) of the anti-Pr2 antibody that was related to the Ag-binding site and was expressed by both the lymphoma and derived cell lines. This unique Id was expressed by the majority of splenic tumor B cells and also was conserved over a period of 4 yr. In this report, the structural basis of IdRI.1 expression was investigated by analysis of Id- variants isolated by flow microfluorimetry using RI.1. Six Id- cell lines that secrete IgM kappa but lack Pr2 specificity were generated from an Id+ cell line, LS2. These lines were shown to be related to LS2 and the lymphoma by karyotype and by restriction fragment analysis of Ig gene rearrangements. Shared and unshared nucleotide substitutions in the VH and VL regions of the six independent \*\*\*clones\*\*\* were used to construct a genealogic tree relating the Id- clonal members to a common Id+ precursor. The tree illustrates that the base changes occurred sequentially, suggesting that

they were introduced by somatic point mutation. Only one VH CDR3 bp difference from the LS2 nucleic acid sequence is common to all Id-sequences, resulting in an amino acid substitution of cysteine 108 to tyrosine. Taken together, these findings suggest that both the expression of IdRI.1 and Ag binding are affected by a single mutation localized to the D region of the anti-Pr2 antibody.

L11 ANSWER 10 OF 20 MEDLINE DUPLICATE 6  
 AN 90187894 MEDLINE  
 DN 90187894 PubMed ID: 1690244  
 TI Anti-idiotypic antibodies recognizing stable epitopes limit the emergence of idiotypic variants in a murine \*\*\*B\*\*\* \*\*\*cell\*\*\*  
 \*\*\*lymphoma\*\*\*  
 AU Weiner G J; Kaminski M S  
 CS Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor 48109.  
 NC 5F23CA08449 (NCI)  
 K08CA01269 (NCI)  
 SO JOURNAL OF IMMUNOLOGY, (1990 Mar 15) 144 (6) 2436-45.  
 Journal code: IFB; 2985117R. ISSN: 0022-1767.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199004  
 ED Entered STN: 19900601  
 Last Updated on STN: 19980206  
 Entered Medline: 19900416  
 AB The emergence of Id variants is a major escape mechanism from anti-Id therapy of human B cell malignancies and of the murine \*\*\*B\*\*\*  
 \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* 38C13. To determine what impact the epitope specificity of anti-Id antibodies has on the prevention of emergence of such Id variants in the 38C13 lymphoma, anti-Id mAb of varying epitope specificity for the Id of 38C13 tumor cells were produced and studied. Some antibodies, produced by immunizing mice with both the wild-type 38C13 IgM and variant IgM, cross-reacted with wild-type 38C13 IgM and with all four members of a panel of variant IgM. These anti-Id did not react with separated 38C13 IgM H or L chains by Western blot, but did react with the cytoplasmic H chain of the surface Ig- variant cell line T2D that expresses the same H chain as wild-type 38C13 in its cytoplasm but does not express any associated L chain. In contrast, anti-Id of narrower specificity did not react with this H chain. This indicated that the broadly cross-reactive antibodies recognized a stable epitope on 38C13 H chain. When a broadly cross-reactive antibody MS11G6 was compared to S1C5, an antibody of narrower specificity, MS11G6, was superior at preventing tumor growth in mice inoculated with 38C13 cells. Moreover, no surface Ig+ variants emerged in escaping tumors in the MS11G6-treated group, whereas such variants were common in the S1C5 treated group. Both anti-Id were of equal efficacy in eliminating wild-type 38C13 cells by using 38C13 cells in tumor inoculums that had just been \*\*\*cloned\*\*\* in vitro, but MS11G6 was also capable of preventing the growth of several surface Ig+ variant cell lines in vivo. We conclude that anti-Id recognizing more stable Id determinants can limit the emergence of Id variants and therefore be more effective therapeutic agents. This finding is of additional importance as additional in vivo and immunophenotypic studies demonstrated that the generation of Id variants was an ongoing process both in \*\*\*cloned\*\*\* parental 38C13 cells and its variants.



L11 ANSWER 11 OF 20 MEDLINE DUPLICATE 7  
 AN 90111038 MEDLINE  
 DN 90111038 PubMed ID: 2104893  
 TI Clonal diversity in human \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* .  
 I. Idiotypic and genetic analysis of lymphoma heterohybrids.  
 AU Rudders R A; Jespersen D L; Zacks J; Sikorski A; DeLellis R A; Krontiris T  
 CS Department of Medicine, New England Medical Center Hospital, Boston, MA  
 02111.  
 NC CA09429 (NCI)  
 CA40725 (NCI)  
 SO JOURNAL OF IMMUNOLOGY, (1990 Jan 1) 144 (1) 396-407.  
 Journal code: IFB; 2985117R. ISSN: 0022-1767.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199002  
 ED Entered STN: 19900328  
 Last Updated on STN: 19900328  
 Entered Medline: 19900209  
 AB Secretory heterohybrid \*\*\*clones\*\*\* from seven pristine human B cell  
 lymphomas of diverse histologic types were established to investigate the  
 question of tumor clonal diversity. We found that in six tumors,  
 heterohybrid-derived Ig showed similar band patterns in IEF; families of  
 anti-Id prepared from tumor Ig reacted uniformly with individual  
 heterohybrids and original tumor; and the V gene loci displayed little  
 variation on Southern analysis. In one patient who was followed with  
 serial multiple site biopsies over a 14-mo period, clonal Id was preserved  
 until the final stage of his disease, in spite of cytotoxic treatment. In  
 a single follicular tumor (J.M.), each of the anti-Id reacted uniformly  
 with the parent tumor and the individual heterohybrids, except that three  
 of six \*\*\*clones\*\*\* failed to react with a single anti-Id family  
 member. A Southern analysis of the VH gene locus revealed an identical  
 gene rearrangement that was shared by the parent tumor and each  
 heterohybrid. However, there was considerable heterogeneity of J.M.  
 heterohybrid Ig in IEF gels, and we demonstrated the production of variant  
 lambda L chains by the heterohybrid \*\*\*clones\*\*\* . One type of lambda L  
 chain had a normal mobility in SDS-PAGE gels but larger lambda variants  
 were produced by four of six heterohybrids. A Southern analysis of the VL  
 gene displayed considerable variation in the type of lambda rearrangement  
 present in the various heterohybrids, suggesting extensive diversity at  
 the VL gene locus. In a second tumor (S.C.) that exhibited uniform anti-Id  
 tumor reactivity we were also able to demonstrate the presence of a second  
 minor tumor cell population (a biclonal tumor). Our data suggest that  
 intraclonal VH variation may vary considerably with lymphoma subtype and  
 mutagenic exposure and that an additional mechanism for generating  
 spontaneous intraclonal heterogeneity is genetic variation at the VL  
 locus.  
  
 L11 ANSWER 12 OF 20 MEDLINE  
 AN 89235235 MEDLINE  
 DN 89235235 PubMed ID: 2523940  
 TI The targeting of CD4+ T lymphocytes to a \*\*\*B\*\*\* \*\*\*cell\*\*\*  
 \*\*\*lymphoma\*\*\* . A comparison of anti-CD3-anti-idiotypic antibody  
 conjugates and antigen-anti-idiotypic antibody conjugates.  
 AU Gravelle M; Ochi A

CS Division of Molecular Immunology and Neurobiology, Mount Sinai Hospital  
Research Institute, Toronto, Ontario, Canada.  
SO JOURNAL OF IMMUNOLOGY, (1989 Jun 1) 142 (11) 4079-84.  
Journal code: IFB; 2985117R. ISSN: 0022-1767.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198906  
ED Entered STN: 19900306  
Last Updated on STN: 19900306  
Entered Medline: 19890622  
AB We have targeted CD4+ cytotoxic Th (Th/c) lymphocytes to a \*\*\*B\*\*\*  
\*\*\*cell\*\*\* \*\*\*lymphoma\*\*\*, through the use of a bispecific antibody  
containing binding sites for both the CD3 complex on the Th/c and the Id  
on the surface Ig of the B lymphoma (anti-CD3-anti-Id). \*\*\*Cloned\*\*\*,  
keyhole limpet hemocyanin (KLH)-specific Th/c cells were nonspecifically  
activated by the anti-CD3-anti-Id conjugate to lyse the Id+ B lymphoma  
A20-HL. This cytotoxicity was not inhibited by antibodies to CD4 or LFA-1  
alpha molecules. The anti-CD3-anti-Id conjugates also induced non-lytic Th  
\*\*\*clones\*\*\* to become cytotoxic, a function not elicited when these  
cells were activated specifically by Ag. We compare this model to our  
previously described system where we targeted the KLH-specific Th/c cells  
to the Id+ B lymphoma A20-HL via a conjugate consisting of KLH covalently  
linked to the anti-Id antibody (KLH-anti-Id). The mechanism involved  
processing and presentation of KLH by the A20-HL target. This Ag-specific  
cytotoxicity was MHC class II restricted and was inhibited by antibodies  
to the CD4 molecule. In both systems, activation of the Th/c cells  
resulted in bystander killing of tumor but not normal targets. These  
results may have important implications for the use of Th/c cells in tumor  
immunotherapy.

L11 ANSWER 13 OF 20 MEDLINE DUPLICATE 8  
AN 90000233 MEDLINE  
DN 90000233 PubMed ID: 2506879  
TI A high incidence of rheumatoid factor \*\*\*idiotypes\*\*\* in monoclonal  
proteins in the serum and in lymphoma cells in patients with Sjogren's  
syndrome.  
AU Sugai S; Shimizu S; Tachibana J; Imaoka S; Konda S  
CS Department of Internal Medicine, Kanazawa Medical University, Ishikawa,  
Japan.  
SO JOURNAL OF AUTOIMMUNITY, (1989 Aug) 2 (4) 471-6.  
Journal code: ADL; 8812164. ISSN: 0896-8411.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198911  
ED Entered STN: 19900328  
Last Updated on STN: 19990129  
Entered Medline: 19891106  
AB Patients with Sjogren's syndrome (SS) develop lymphoproliferative  
disorders such as monoclonal gammopathies and non-Hodgkin's lymphomas.  
Cross-reactive \*\*\*idiotypes\*\*\* (CRI) were studied in 22 serum  
monoclonal immunoglobulins (Igs) and in cytoplasmic Ig in four \*\*\*B\*\*\*  
- \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* cells in patients with SS. This was  
done by utilizing monoclonal anti-idiotypic antibodies which were produced

against monoclonal rheumatoid factors (RF) derived from three patients with SS and one patient with Waldenstrom's macroglobulinemia. By the Western blotting or dot immunobinding technique, CRI was detected not only in monoclonal RFs but in monoclonal Igs which had different heavy- or light-chains from the original monoclonal RF used for immunization. A higher incidence of CRI was found in 22 monoclonal Igs associated with SS than in 27 monoclonal Igs in patients with Waldenstrom's macroglobulinemia, multiple myeloma or malignant lymphoma. In four patients with malignant lymphoma associated with SS, three showed one or three CRI in the lymphoma cells, whereas only two out of 20 patients with other malignant lymphoma showed CRI, demonstrating a significant difference between two groups. These data indicate that monoclonal proliferation of B-cell lineage in patients with SS, benign or malignant, takes place more often among RF-producing \*\*\*clones\*\*\* than other B-cell disorders.

L11 ANSWER 14 OF 20 MEDLINE  
 AN 89310348 MEDLINE  
 DN 89310348 PubMed ID: 2501443  
 TI Functional immunoglobulin light chain genes are replaced by ongoing rearrangements of germline V kappa genes to downstream J kappa segment in a murine B cell line.  
 AU Levy S; Campbell M J; Levy R  
 CS Department of Medicine, Stanford University School of Medicine, California 94305.  
 NC AI-07290 (NIAID)  
 CA-33399 (NCI)  
 CA-34233 (NCI)  
 +  
 SO JOURNAL OF EXPERIMENTAL MEDICINE, (1989 Jul 1) 170 (1) 1-13.  
 Journal code: I2V; 2985109R. ISSN: 0022-1007.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198908  
 ED Entered STN: 19900309  
 Last Updated on STN: 19970203  
 Entered Medline: 19890811  
 AB A murine \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* (38C13) was subjected to immunoselection with mAbs directed against the idiotypic determinants of its cell surface Ig. Variants emerged with altered Ig receptors containing identical heavy chains but different light chains. The functional light chain genes in these variants were composed of V kappa segments drawn from the V kappa Ox-1 family, which had replaced the V kappa gene expressed by the parental tumor by rearranging to downstream J kappa segments. Rearrangement at the kappa locus continued to occur spontaneously, giving rise to secondary and tertiary variants at a rate of  $1.9 \times 10^{-4}$  per cell per generation. Variants were isolated that had ceased production of surface Ig but went on to rearrange again and to become surface Ig+. The Ig- state may be an intermediate step providing a stimulus for continued rearrangement. This process provides an additional mechanism for generating diversity within B cell \*\*\*clones\*\*\* and expands the use of the available repertoire of Ig genes.

L11 ANSWER 15 OF 20 MEDLINE DUPLICATE 9  
 AN 88269859 MEDLINE

DN 88269859 PubMed ID: 3291988  
 TI Bone marrow origin of a \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* .  
 AU Bertoli L F; Kubagawa H; Borzillo G V; Burrows P D; Schreeder M T; Carroll A J; Cooper M D  
 CS Division of Developmental and Clinical Immunology, University of Alabama, Birmingham 35294.  
 NC CA 01005 (NCI)  
 CA 13148 (NCI)  
 CA 16673 (NCI)  
 SO BLOOD, (1988 Jul) 72 (1) 94-101.  
 Journal code: A8G; 7603509. ISSN: 0006-4971.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 198808  
 ED Entered STN: 19900308  
 Last Updated on STN: 19970203  
 Entered Medline: 19880819  
 AB To search for precursors of the neoplastic B cells in a patient with a nodular lymphoma, we produced a monoclonal antibody to a variable region idiotope on the lymphoma IgM heavy chain. Clonal ancestors of the lymphoma cells were identified by this marker among bone marrow pre-B cells (5% to 26%). A second antiidiotype (anti-Id) antibody specific for the complete lymphoma IgM kappa recognized 10% of B cells in bone marrow and blood and greater than 95% of B cells in lymphomatous lymph nodes, including one obtained after tumor conversion to a diffuse large cell lymphoma. Immunoglobulin gene analysis surprisingly revealed expansion of multiple \*\*\*clones\*\*\* of early B lineage cells in bone marrow, including members of the neoplastic clone. The data suggest that this lymphoma arose through a progression of transformational events beginning in bone marrow: first, creation of an oligoclonal pre-neoplastic pool of pre-B cells, subsequent conversion of a single subclone into low grade neoplastic B cells that homed to the lymph node follicles, and later progression to a more invasive form of the \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* .

L11 ANSWER 16 OF 20 MEDLINE DUPLICATE 10  
 AN 87260927 MEDLINE  
 DN 87260927 PubMed ID: 3496601  
 TI Retention of an idiotypic determinant in a human \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* undergoing immunoglobulin variable-region mutation.  
 AU Kon S; Levy S; Levy R  
 NC CA33399 (NCI)  
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1987 Jul) 84 (14) 5053-7.  
 Journal code: PV3; 7505876. ISSN: 0027-8424.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-M16948; GENBANK-M16949; GENBANK-M16950; GENBANK-M16951; GENBANK-M16952; GENBANK-M16953  
 EM 198708  
 ED Entered STN: 19900305  
 Last Updated on STN: 19970203  
 Entered Medline: 19870820  
 AB Tumor cells from a patient with \*\*\*B\*\*\* - \*\*\*cell\*\*\*

\*\*\*lymphoma\*\*\* were fused with a mouse myeloma cell line. A set of heterohybridomas was thus derived, each of which represented a separate clonal derivative from the tumor cell population. The immunoglobulins secreted by these cell lines reacted variably with a panel of anti-idiotypic antibodies, indicating that the tumor was heterogeneous; however, one antibody, 4D6, reacted strongly with the product of all the heterohybridomas. cDNA for the immunoglobulin heavy chain variable-region genes expressed in these heterohybridomas was \*\*\*cloned\*\*\* and sequenced. Comparison of these sequences indicated that the cells expressing them were clonally related but that they had undergone considerable mutation. Despite mutation, the cells in this tumor population continued to express a functional immunoglobulin molecule and to retain, over a span of 3 years, the idiotypic determinant defined by the 4D6 monoclonal antibody. Thus a selective force existed within the host to retain tumor cells bearing an immunoglobulin molecule with a particular idiotypic structure.

L11 ANSWER 17 OF 20 MEDLINE DUPLICATE 11  
 AN 85159426 MEDLINE  
 DN 85159426 PubMed ID: 2984307  
 TI Frequent biclonality and Ig gene alterations among B cell lymphomas that show multiple histologic forms.  
 AU Siegelman M H; Cleary M L; Warnke R; Sklar J  
 NC CA 34233 (NCI)  
 SO JOURNAL OF EXPERIMENTAL MEDICINE, (1985 Apr 1) 161 (4) 850-63.  
 Journal code: I2V; 2985109R. ISSN: 0022-1007.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198505  
 ED Entered STN: 19900320  
 Last Updated on STN: 19970203  
 Entered Medline: 19850513  
 AB Configurations of Ig gene DNA were examined in multiple biopsy specimens from seven cases of human \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* that showed histologic differences among the specimens within each case. Analysis by Southern blot hybridizations with DNA probes for each of the three Ig loci revealed that the configurations of DNA within these loci were identical among the specimens in two of the cases. This result indicated the monoclonality of these lymphomas, despite differences in histology between biopsy specimens. In contrast, no common nongerm-line configurations of Ig gene DNA were detected among multiple biopsies in each of three other cases. Therefore, different histologies correlated with separate \*\*\*clones\*\*\* of proliferating B cells in these cases. In the last two cases, the configurations of light chain gene DNA were the same among biopsies in each case, consistent with a monoclonal origin in both lymphomas. However, differences were detected in the configuration of the heavy chain gene DNA. Analysis with a series of DNA probes of the mu heavy chain region indicated that the differences in the DNA configurations of the heavy chain genes from the biopsies probably arose from postrearrangement deletions of either the switch or constant regions of the mu gene. These studies indicate that, contrary to the conventional belief, individual tumors that contain different histologic types of lymphoma within the same patient frequently arise from separate \*\*\*clones\*\*\* of neoplastic cells. Furthermore, the heavy chain genes of monoclonal tumors may show postrearrangement deletions, often resulting

from instability of DNA sequences within or around the mu switch region.

L11 ANSWER 18 OF 20 MEDLINE DUPLICATE 12  
AN 85133381 MEDLINE  
DN 85133381 PubMed ID: 2579186  
TI Induction of immunoglobulin isotype switching in cultured I.29 B lymphoma cells. Characterization of the accompanying rearrangements of heavy chain genes.  
AU Stavnezer J; Sirlin S; Abbott J  
NC A117558 (NIAID)  
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1985 Mar 1) 161 (3) 577-601.  
Journal code: I2V; 2985109R. ISSN: 0022-1007.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198504  
ED Entered STN: 19900320  
Last Updated on STN: 19970203  
Entered Medline: 19850404  
AB The murine \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* I.29 contains cells expressing surface IgM or IgA with identical heavy chain variable regions (9, 25, and D. Klein and J. Stavnezer, unpublished data). Purified IgM+ cells from the lymphoma have been adapted to culture and induced to switch to IgA, IgE, or IgG2 by treatment with lipopolysaccharide (LPS) or by treatment with a monoclonal anti-I.29 antiidiotype plus LPS.  
\*\*\*Clones\*\*\* of IgM+ cells have been obtained and induced to switch. Under optimal conditions, 30% of the cells in the culture expressed IgA 8 d after the inducers were added, and by 15 d 90% of the cells were IgA+. In actively switching cultures, up to 50% of the cells whose cytoplasm stained positively with anti-IgA stained simultaneously with anti-IgM, which indicates that the appearance of IgA+ cells in the cultures was due to isotype switching and not to clonal outgrowth. Examination by Southern blotting experiments of the Ig heavy chain genes in I.29 cells before and after switching revealed that isotype switching was accompanied by DNA recombinations that occurred within or immediately 5' to the tandemly repeated switch sequences. Within 3 d after the addition of inducers of switching, the nonexpressed chromosome underwent a variety of deletions or expansions within the S mu region, and a portion of the S alpha regions had undergone a 0.9-kb deletion. In cultures that contained at least 12% IgA+ cells, rearranged, expressed alpha genes, produced by recombination between the S mu region within the expressed mu gene and the S alpha region, were detected.

L11 ANSWER 19 OF 20 MEDLINE DUPLICATE 13  
AN 85236147 MEDLINE  
DN 85236147 PubMed ID: 3925067  
TI Syngeneic antiidiotypic immune responses to a \*\*\*B\*\*\* \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* . Comparison between heavy chain hypervariable region peptides and intact Ig as immunogens.  
AU Thielemans K; Rothbard J B; Levy S; Levy R  
NC CA 21223 (NCI)  
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1985 Jul 1) 162 (1) 19-34. Ref: 40  
Journal code: I2V; 2985109R. ISSN: 0022-1007.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LA English  
 FS Priority Journals  
 OS GENBANK-X02676  
 EM 198508  
 ED Entered STN: 19900320  
 Last Updated on STN: 19970203  
 Entered Medline: 19850815  
 AB The nucleic acid sequence of the heavy chain variable region (VH) expressed by 38C13, a B cell tumor of C3H origin, was determined by a combination of direct (messenger RNA) mRNA sequencing by primer extension and complementary DNA (cDNA) isolation and sequencing in M13. The VH amino acid sequence was deduced, and hypervariable regions were identified. From an analysis of predicted secondary structure, regions of predicted antigenicity were chosen, and a series of synthetic peptides corresponding to CDR2 and CDR3 (complementarity-determining region) were produced. These peptides were coupled to protein carriers and used to immunize syngeneic C3H mice. All peptides gave rise to a vigorous antibody response. However, only the CDR3 peptides induced antibodies that crossreacted with the isolated H chain protein. Only one CDR3 peptide induced antibody-producing \*\*\*clones\*\*\*, isolated as hybridomas, that reacted with the intact IgM protein. However, the appearance of these \*\*\*clones\*\*\* was a low-frequency event. All antibodies reacting with the H chain or the intact IgM protein were idiotypically specific for 38C13. These monoclonal antiidiotypic (anti-Id) antibodies, raised against CDR3 peptides, gave strong reactions in enzyme-linked immunosorbent assays and immunoblots, but they were of low affinity compared to syngeneic anti-Id raised against the intact IgM protein. Moreover, while the intact IgM was capable of inducing tumor immunity, the CDR peptides were not able to do so.

L11 ANSWER 20 OF 20 MEDLINE DUPLICATE 14  
 AN 82222262 MEDLINE  
 DN 82222262 PubMed ID: 6806821  
 TI Simultaneous expression of immunoglobulin mu and delta heavy chains by a \*\*\*cloned\*\*\* \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* : a single copy of the VH gene is shared by two adjacent CH genes.  
 AU Knapp M R; Liu C P; Newell N; Ward R B; Tucker P W; Strober S; Blattner F  
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1982 May) 79 (9) 2996-3000.  
 Journal code: PV3; 7505876. ISSN: 0027-8424.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-J00494  
 EM 198208  
 ED Entered STN: 19900317  
 Last Updated on STN: 19900317  
 Entered Medline: 19820814  
 AB The \*\*\*cloned\*\*\* murine \*\*\*B\*\*\* - \*\*\*cell\*\*\* \*\*\*lymphoma\*\*\* line (BCL1) that expresses surface IgM and IgD is considered to be a model for the immunoglobulin gene expression of the mature virgin B cell. Of particular interest is the mechanism by which a single VH gene is shared by two CH genes. We examined the organization of the immunoglobulin heavy chain genes in BCL1 DNA. A single arrangement of CH genes was found with the expressed VHDJH gene complex just 5' to the Cmu gene. The complete DNA sequence of the VH gene was determined. No rearrangement occurred in the intervening DNA between the JH and C mu genes or between the C mu and C

delta genes. We conclude that dual expression of mu and delta heavy chains using a single VH gene is accomplished by alternate processing of a primary transcript that encompasses the the VHDJH complex and both CH genes.